

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

IN RE APPLICATION OF: Tom TSANG, et al.

SERIAL NO: New U.S. Application

FILED: Herewith

FOR: HYPERTHERMIC INDUCIBLE EXPRESSION VECTORS FOR GENE THERAPY AND METHODS OF USE THEREOF

**INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR 1.97**

COMMISSIONER FOR PATENTS  
ALEXANDRIA, VIRGINIA 22313

SIR:

Applicant(s) wish to disclose the following information.

**REFERENCES**

- ☒ The applicant(s) wish to make of record the references listed on the attached form PTO-1449 were mentioned in Parent Application, Serial No. 09/185,243 filed November 3, 1998.
- ☐ A check or credit card payment form is attached in the amount required under 37 CFR §1.17(p).

**RELATED CASES**

- ☐ Attached is a list of applicant's pending application(s) or issued patent(s) which may be related to the present application. A copy of the patent(s), together with a copy of the claims and drawings of the pending application(s) is attached along with PTO 1449.
- ☐ A check or credit card payment form is attached in the amount required under 37 CFR §1.17(p).

**CERTIFICATION**

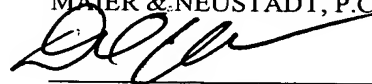
- ☐ Each item of information contained in this information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement.
- ☐ No item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application or, to the knowledge of the undersigned, having made reasonable inquiry, was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of this statement.

**DEPOSIT ACCOUNT**

- ☒ Please charge any additional fees for the papers being filed herewith and for which no check or credit card payment is enclosed herewith, or credit any overpayment to deposit account number 15-0030. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.



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Registration No. 45,518

Form PTO 1449  
(Modified)U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY DOCKET NO.  
246392US20CONTSERIAL NO.  
New U.S. Application

## LIST OF REFERENCES CITED BY APPLICANT

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Tom TSANG, et al.FILING DATE  
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## U.S. PATENT DOCUMENTS

| EXAMINER<br>INITIAL |    | DOCUMENT<br>NUMBER | DATE     | NAME                 | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|----|--------------------|----------|----------------------|-------|--------------|-------------------------------|
|                     | AA | 5,614,381          | 3/97     | Bromley, et al.      |       |              |                               |
|                     | AB | 5,646,010          | 7/97     | Bromley, et al.      |       |              |                               |
|                     | AC | 3,991,770          | 11/16/76 | LeVeen               |       |              |                               |
|                     | AD | 5,889,169          | 3/30/99  | Beach et al.         |       |              |                               |
|                     | AE | 5,877,010          | 3/2/99   | Loeb et al.          |       |              |                               |
|                     | AF | 5,817,492          | 10/6/98  | Saito et al.         |       |              |                               |
|                     | AG | 5,583,038          | 12/10/96 | Stover               |       |              |                               |
|                     | AH | 5,834,306          | 12/23/94 | Webster et al.       |       |              |                               |
|                     | AI | 5,814,482          | 9/29/98  | Dubensky, Jr. et al. |       |              |                               |
|                     | AJ | 5,770,414          | 6/23/98  | Gage et al.          |       |              |                               |
|                     | AK |                    |          |                      |       |              |                               |

## FOREIGN PATENT DOCUMENTS

|  |    | DOCUMENT<br>NUMBER | DATE     | COUNTRY | TRANSLATION |    |
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|  |    |                    |          |         | YES         | NO |
|  | AO | 0 118 393          | 9/84     | Europe  |             |    |
|  | AP | 0 299 127          | 1/89     | Europe  |             |    |
|  | AQ | 89/00603           | 1/89     | WIPO    |             |    |
|  | AR | 0 455 424          | 11/91    | Europe  |             |    |
|  | AS | 95/24491           | 9/95     | WIPO    |             |    |
|  | AT | 89/10412           | 11/2/89  | WIPO    |             |    |
|  | AU | 95/09913           | 4/13/95  | WIPO    |             |    |
|  | AV | 0,342,926          | 11/12/89 | Europe  |             |    |

## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

|  |    |   |  |  |  |  |
|--|----|---|--|--|--|--|
|  | AW | Blackburn et al., "Adenoviral-mediated transfer of a heat-inducible double suicide gene into prostate carcinoma cells, "Cancer Research, 58:1358-1362 (1998). |  |  |  |  |
|  | AX | Clackson, T., "Controlling mammalian gene expression with small molecules, "Current Opinion in Chemical Biology, 1:210-218 (1997).                            |  |  |  |  |
|  | AY | Dachs et al., "Targeting gene expression to hypoxic tumor cells, "Nature Medicine, 3:515-520 (1997).  |  |  |  |  |
|  | AZ | Dreano et al., "Antibody formation against heat-induced gene products expressed in animals, "Biotechnology, p. 1340-1343 (1988)                               |  |  |  | <input type="checkbox"/> Additional References sheet(s) attached |

Examiner

Date Considered

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## BOREIGN PATENT DOCUMENTS

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|  |    |                    |      |         | YES         | NO |
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## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

|  |    |  |  |  |  |  |
|--|----|--|--|--|--|--|
|  | BW | Emerman et al., "The specificity of the human immunodeficiency virus type 2 transactivator is different from that of human immunodeficiency virus type 1," <i>The EMBO Journal</i> , 6:3755-3760 (1987).   |  |  |  |  |
|  | BX | Finch et al., "Overexpression of three ubiquitin genes in mouse epidermal tumors is associated with enhanced cellular proliferation and stress," <i>Cell Growth &amp; Differentiation</i> , 3:269-278 (1992)   |  |  |  |  |
|  | BY | Friedmann, T., "Overcoming the obstacles: treating disease by providing needed genes remains a compelling idea, but clinical and basic researchers still have much to do before gene therapy can live up to its promise," <i>Scientific American</i> , 276-96-101 (1997) |  |  |  |  |
|  | BZ | Gazit et al., "Use of the stress-inducible grp78/BiP promoter in targeting high level gene expression in fibrosarcoma <i>in vivo</i> ," <i>Cancer Research</i> , 55:1660-1663 (1995)   |  |  |  | <input type="checkbox"/> Additional References sheet(s) attached |

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| EXAMINER<br>INITIAL  |    | DOCUMENT<br>NUMBER  | DATE | NAME                                     | CLASS                                      | SUB<br>CLASS    | FILING DATE<br>IF APPROPRIATE                                    |  |  |
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| <b>OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)</b>   |    |   |      |  |  |                 |  |  |  |
|  | CW | Desiderio et al., "Effects of polyamine imbalance on the induction of stress genes in hepatocarcinoma cells exposed to heat shock", Hepatology, 24:150-156 (1996)             |      |  |  |                 |  |  |  |
|  | CX | Mitchell et al., "Involvement of the polyamine transport system in cellular uptake of the radioprotectants WR-1065 and WR-33278", Carcinogenesis, 12:: 3063-3068 (1995)       |      |  |  |                 |  |  |  |
|  | CY | Suzuki et al., "Effect of low-dose preirradiation on induction of the HSP70B-LacZ fusion gene in human cells treated with heat shock", Radiation Research, 2: 195-201 (1998). |      |  |  |                 |  |  |  |
|  | CZ | Vasanwala et al., "A novel gene expression vector induced by heat shock, chemotherapy and radiation", Cancer Gene Therapy, 4: p. 28, (1997)                                   |      |  |  |                 | <input type="checkbox"/> Additional References sheet(s) attached |  |  |
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| <b>OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)</b>   |    |  |      |  |  |  |   |  |
|  | DW | Vasanwala et al., "High Level IL-2 expression vectors using HIV LTR in human colon carcinoma cell line", Proceedings of the American Association for Cancer Research Annual Meeting, 38: p. 33, (April 16, 1997) |      |  |  |  |   |  |
|  | DX | Gomer et al., "Photodynamic therapy-mediated oxidative stress can induce expression of heat shock proteins, "Cancer Research, 56:2355-2360 (1996)  |      |  |  |  |   |  |
|  | DY | Harisiadis et al., "Carcinoma of the prostate: treatment with external radiotherapy, "Cancer, 41:2131-2142 (1978).   |      |  |  |  |   |  |
|  | DZ | Iida et al., "Inducible gene expression by retrovirus-mediated transfer of a modified tetracycline-regulated system, "Journal of Virology, 70:6054-6059 (1996)   |      |  |  | <input type="checkbox"/> Additional References sheet(s) attached |   |  |
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## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

|  |    |   |  |  |  |  |
|--|----|---|--|--|--|--|
|  | EW | Leppa et al., "Heat shock response – pathophysiological implications, "Ann. Med., 29:73-78 (1997)   |  |  |  |  |
|  | EX | Leung et al., "The human heat-shock protein family, "Biochem. J., 267:125-132 (1990)  |  |  |  |  |
|  | EY | Lindholm et al., "Microwave-induced hyperthermia and radiotherapy in human superficial tumors: clinical results with a comparative study of combined treatment versus radiotherapy alone, "Recent Results in Cancer Research, 107:152-156 (1988). |  |  |  |  |
|  | EZ | Little et al., "The glucose-regulated proteins (GRP78 and GRP94): functions, gene regulation, and applications, "Critical Reviews in Eukaryotic Gene Expression, 4(1):1-18 (1994)   |  |  |  | <input type="checkbox"/> Additional References sheet(s) attached |

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## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

|  |    |   |  |
|--|----|---|--|
|  | FW | Madio et al., "On the feasibility of MRI-guided focused ultrasound for local induction of gene expression," <i>Journal of Magnetic Resonance Imaging</i> , 8:101-104 (1998)   |  |
|  | FY | Oleson et al., "Eugene Robertson Special Lecture. Hyperthermia from the clinic to the laboratory: a hypothesis," <i>International Journal of Hyperthermia</i> , 11:315-322 (1995)   |  |
|  | FY | Pennington et al., "Quantitative assessment of heat inducible gene expression," <i>Sixth International Conference on Gene Therapy of Cancer</i> , November 20-22, 1997.   |  |
|  | FZ | Roigas et al., "Effects of combined treatment of chemotherapeutics and hyperthermia on survival and the regulation of heat shock proteins in Dunning R3327 prostate carcinoma cells," <i>The Prostate</i> , 34:195-202 (1998) | <input type="checkbox"/> Additional References sheet(s) attached |

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|  | GO |                    |      |         |             |    |
|  | GP |                    |      |         |             |    |
|  | GQ |                    |      |         |             |    |
|  | GR |                    |      |         |             |    |
|  | GS |                    |      |         |             |    |
|  | GT |                    |      |         |             |    |
|  | GU |                    |      |         |             |    |
|  | GV |                    |      |         |             |    |

## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

|  |    |   |  |
|--|----|---|--|
|  | GW | Sapareto et al., "Effects of hyperthermia on survival and progression of Chinese hamster ovary cells," Cancer Research, 38:393-400 (1978)   |  |
|  | GX | Sarge, K., "Regulation of HSF1 activation and Hsp expression in mouse tissues under physiological stress conditions," Annals of the New York Academy of Sciences, 851:112-116 (1998)                                  |  |
|  | GY | Schweinfest et al., "A heat-shock-inducible eukaryotic expression vector," Gene, 71:207-210 (1988)  |  |
|  | GZ | Scott et al., "Local hyperthermia in combination with definitive radiotherapy: increased tumor clearance, reduced recurrence rate in extended follow-up," Int. J. Radiation Oncology Biol. Phys., 10:2119-2123 (1984) | <input type="checkbox"/> Additional References sheet(s) attached |

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|                     | HA |                    |      |      |       |              |                               |
|                     | HB |                    |      |      |       |              |                               |
|                     | HC |                    |      |      |       |              |                               |
|                     | HD |                    |      |      |       |              |                               |
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|                     | HF |                    |      |      |       |              |                               |
|                     | HG |                    |      |      |       |              |                               |
|                     | HH |                    |      |      |       |              |                               |
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|  |    | DOCUMENT<br>NUMBER | DATE | COUNTRY | TRANSLATION |    |
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|  |    |                    |      |         | YES         | NO |
|  | HQ |                    |      |         |             |    |
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|  | HQ |                    |      |         |             |    |
|  | HR |                    |      |         |             |    |
|  | HS |                    |      |         |             |    |
|  | HT |                    |      |         |             |    |
|  | HU |                    |      |         |             |    |
|  | HV |                    |      |         |             |    |

## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

|  |    |   |  |
|--|----|---|--|
|  | HW | Sodroski et al., "A transcriptional activator protein encoded by the x-for region of the human T-cell leukemia virus," Science, 228-1430-1434 (1985)                |  |
|  | HX | Tsang et al., "Mammalian expression vector with two multiple cloning sites for expression of two foreign genes," Bio Techniques, 22:68 (1997)                       |  |
|  | HY | Tsang et al., "New vectors for augmented levels of heat inducible gene expression," Sixth International Conference on Gene Therapy of Cancer, November 20-22 (1997) |  |
|  | HZ | Tsang et al., Simple method for adapting DNA fragments and PCR products to all of the commonly used restriction sites, "Bio Techniques, 20:51-52 (1996)             | <input type="checkbox"/> Additional References sheet(s) attached |

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|                     | IJ |                    |      |      |       |              |                               |
|                     | IK |                    |      |      |       |              |                               |
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|  |    |                    |      |         | YES         | NO |
|  | IO |                    |      |         |             |    |
|  | IP |                    |      |         |             |    |
|  | IO |                    |      |         |             |    |
|  | IR |                    |      |         |             |    |
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|  | IT |                    |      |         |             |    |
|  | IU |                    |      |         |             |    |
|  | IV |                    |      |         |             |    |

## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

|  |    |  |
|--|----|--|
|  | IW | Varley et al., "A two-component expression system that responds to inflammatory stimuli <i>in vivo</i> ", <i>Nature Biotechnology</i> , 15:1002-1006 (1997).         |
|  | IX | Walther et al., "Cell type specific and inducible promoters for vectors in gene therapy as an approach for cell targeting", <i>J. Mol. Med.</i> , 74:379-392 (1996). |
|  | IY | Wu, C. "Heat shock transcription factors: structure and regulation", <i>Annu. Rev Cell Dev. Biol.</i> , 11:441-69 (1995)   |
|  | IZ | Tewari et al., <i>Biochem. Biophys. Acta</i> , 1209:293-295  |

☐ Additional References sheet(s) attached

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|                     | JA |                    |      |      |       |              |                               |
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|                     | JC |                    |      |      |       |              |                               |
|                     | JD |                    |      |      |       |              |                               |
|                     | JF |                    |      |      |       |              |                               |
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|                     | JG |                    |      |      |       |              |                               |
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|                     | JI |                    |      |      |       |              |                               |
|                     | JJ |                    |      |      |       |              |                               |
|                     | JK |                    |      |      |       |              |                               |
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|  |    |                    |      |         | YES         | NO |
|  | JO |                    |      |         |             |    |
|  | JP |                    |      |         |             |    |
|  | JQ |                    |      |         |             |    |
|  | JR |                    |      |         |             |    |
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|  | JT |                    |      |         |             |    |
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## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

|  |    |   |  |
|--|----|---|--|
|  | JW | Agrawal, TIBTECH, 14:376-387                        |  |
|  | JX | Gaestel et al., Gene, 128:279-283                   |  |
|  | JY | Dale et al., Gene, 172:279-284                      |  |
|  | JZ | Hickey et al., Nucleic Acids Research, 14:4127-4145 | <input type="checkbox"/> Additional References sheet(s) attached |

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|                     | JK |                    |      |      |       |              |                               |
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|  | JT |                    |      |         |             |    |
|  | JU |                    |      |         |             |    |
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## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

|  |    |   |  |
|--|----|---|--|
|  | JW | Gura, Science, 278:1041-1042                        |  |
|  | JX | Gomez-Navarro et al, European J. Cancer, 35:867-885 |  |
|  | JY | Leitner et al., Vaccine, 18:765-777                 |  |
|  | JZ | Branch, TIBS, 23:45-50                              | <input type="checkbox"/> Additional References sheet(s) attached |

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|                     | KA |                    |      |      |       |              |                               |
|                     | KB |                    |      |      |       |              |                               |
|                     | KC |                    |      |      |       |              |                               |
|                     | KD |                    |      |      |       |              |                               |
|                     | KE |                    |      |      |       |              |                               |
|                     | KF |                    |      |      |       |              |                               |
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|                     | KI |                    |      |      |       |              |                               |
|                     | KJ |                    |      |      |       |              |                               |
|                     | KK |                    |      |      |       |              |                               |
|                     | KL |                    |      |      |       |              |                               |
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|  |    |                    |      |         | YES         | NO |
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|  | KP |                    |      |         |             |    |
|  | KQ |                    |      |         |             |    |
|  | KR |                    |      |         |             |    |
|  | KS |                    |      |         |             |    |
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|  | KV |                    |      |         |             |    |

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|  |    |  |
|--|----|--|
|  | KW | Verma et al., Nature, 389:239-242  |
|  | KX | Ledley, Pharmaceutical Research, 13:1595-1614  |
|  | KY | Hancock, in Methods in Molecular Biology-8, Practical Molecular Virology, Viral Vectors for Gene Expression, ed. M. Collins, Humana Press, Inc., New Jersey, Chapter 14, pages 153-158         |
|  | KZ | Talavera et al., in Methods in Molecular Biology-8, Practical Molecular Virology, Viral Vectors for Gene Expression, ed. M. Collins, Humana Press, Inc., New Jersey, Chapter 21, pages 235-248 |

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| <b>OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)</b>   |    |   |      |  |  |              |  |  |
|  | LW | Orkin et al., in Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy, December 7   |      |  |  |              |  |  |
|  | LX | Brady et al., "Specific ablation of human immunodeficiency virus Tat-expressing cells by conditionally toxic retroviruses", Proc. Natl. Acad. Sci. USA 91:365-369, Jan 1994 |      |  |  |              |  |  |
|  | LY |   |      |  |  |              |  |  |
|  | LZ |   |      |  |  |              | <input type="checkbox"/> Additional References sheet(s) attached |  |
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